International Journal of Infectious Diseases (2008) **12**, 43—46

http://intl.elsevierhealth.com/journals/ijid

Efficacy of measles and rubella vaccination one year after the nationwide campaign in Shiraz, Iran

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Received 1 November 2006; received in revised form 24 February 2007; accepted 1 March 2007
Corresponding Editor: Jane Zuckerman, London, UK

KEYWORDS
Measles;
Rubella;
Vaccine efficacy;
Iran

Summary
Background: The World Health Organization target for measles elimination in the Eastern Mediterranean Region was established in 2010. In Iran, the national measles—rubella campaign, targeting individuals aged 5—25 years, was initiated in December 2003.
Methods: To evaluate the impact of the campaign after one year, 909 serum samples were collected in Shiraz, southern Iran, from a population aged 6—26 years, divided into five groups according to age. IgG antibodies were tested using ELISA for the measles and rubella antibodies, and the plaque reduction neutralization test (PRNT; measles) was used for samples with equivocal results.
Results: Measles protective immunity reached 80.6%, 72.7%, 84.9%, and 87.5% and rubella immunity reached 91.0%, 99.6%, 99.6%, and 97.0% for the age groups 6—10, 11—15, 16—20, and 20—26 years, respectively. Seropositivity to the rubella virus in this population was high, especially in women of childbearing age (98.9%), thereby preventing congenital rubella infections. However for measles, it was significantly lower than the rate required to achieve ≥95% coverage for elimination.
Conclusions: These data indicate that an increase in immunization coverage by supplementary administration of a second dose of measles vaccine is needed to interrupt the endemic transmission of the measles virus.

Introduction

Measles is a notable cause of mortality and morbidity in children and is responsible for 4% of the six million annual deaths in children under five years of age. Ninety-eight percent of these deaths occur in developing countries.[1]

Although the virus is highly contagious and easily transmitted, measles can be effectively prevented by attenuated live vaccine. Prevention of measles using vaccination is still a most important task in developing countries. Target dates for measles elimination in three World Health Organization (WHO) regions, the Americas, Europe, and the Eastern Mediterranean Region (EMR), were set for 2000, 2007, and 2010, respectively.[2]

Rubella is considered a mild viral infectious disease, with man the only known reservoir; congenital rubella syndrome (CRS) is the only remarkable complication of the disease.

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1201-9712/$32.00
doi:10.1016/j.ijid.2007.03.013

WHO reports reveal that a minimum of 100 000 cases of CRS occur annually worldwide,[3] but the true incidence may be more than double that estimate.[4] Prevention of CRS is best achieved through widespread immunization, resulting in a high seropositivity rate in pregnant women.

In 2003, the Iranian campaign was the world's largest vaccination operation. Measles and rubella (MR) vaccines (measles, Edmonston Zagreb strain; rubella, RA27/3 strain; Serum Institute of India Ltd) were administered to more than 33 million people aged between 5 and 25 years, in less than one month. The decline in measles incidence due to the vaccination program and the recent campaign has been observed in children, however cases of the disease still emerge. This might be due to primary vaccine failure, as well as immigration from neighboring countries with low vaccine coverage.[5] The frequency of primary vaccine failure is variable and has been shown to be a function of age at the time of vaccination, the number of doses, the immunogenicity of the strain of the virus used to manufacture the vaccine, the geographic region, and insufficient maintenance of the cold chain.[6]

Therefore, a surveillance program should now be established to monitor the impact of vaccination. The aim of this study was to survey the efficacy of the measles and rubella vaccination one year after the national campaign in Shiraz, Iran.

Materials and methods

Samples

Sera were collected over the period February 2004 to June 2005 from 909 individuals with an age range of 6–26 years among the population of Shiraz, a city in southern Iran with a population of 1.1 million (according to a 2005 estimate). The specimens belonged to 505 females and 404 males; selection was by the random sampling method. The cases were divided into five groups according to their ages. Considering the current population of Shiraz, the minimum sample size required for the current study was calculated to be 896 with a 5% error and 90% confidence interval.

A questionnaire was used to collect demographic information including age, sex, previous history of measles, and vaccination in the recent campaign.

ELISA for measles and rubella specific IgG detection

The sera were examined using solid phase ELISA IgG kits (IBL, Immuno-Biological Laboratories, Germany) for quantitative determination of IgG antibodies against measles and rubella. Testing was performed according to the manufacturer's instructions. 'Non-immune' was defined as a measles IgG concentration of <8 U/ml and a rubella IgG concentration of <10 IU/ml. Values between 8 and 12 U/ml for measles and 10 and 15 IU/ml for rubella were regarded as 'equivocal', and values of >10 U/ml for measles and >15 IU/ml for rubella were considered as 'immune'. The sensitivity and specificity of tests for measles and rubella were similar with values of 95% and 98%, respectively. The sera with equivocal antibody values for measles detected by ELISA were retested by plaque reduction neutralization test.

Plaque reduction neutralization test (PRNT)

All sera with equivocal measles antibody values were retested by the PRNT based on the standard protocol.[7] Briefly, serum samples were diluted two-fold from 1:8 to 1:256, mixed with an equal volume of the vaccine strain virus (Edmonston Zagreb strain) containing 20–30 PFU, and incubated at 36 °C for 2.5 h. Serum/virus mixtures were transferred to 16-mm culture plates containing a vero cell monolayer. These plates were incubated at 37 °C in a humidified CO_2 incubator for 1 h. The inoculums were then removed and replaced with overlay medium. The plates were incubated for five days at 36 °C and the plaques were counted. The end-point for the test was the highest dilution of serum that reduced the number of plaques by 50%. A PRNT titer of >1:120 was considered to be a level of antibody to provide protection against measles.[8]

Statistical analysis

Statistical analysis was carried out using SPSS software version 11 (Chicago, IL, USA) using Chi-square and regression analysis tests. A p-value of less than 0.05 was considered significant.

Results

Nine hundred and nine samples from the five age groups were tested by ELISA for measles and rubella. One hundred and twenty samples with equivocal results for measles were re-examined with PRNT (Table 1). No hemagglutination inhibition test was performed for the equivocal cases of rubella, due to the low number of cases (seven samples); for the equivocal measles cases (120 samples) it was worthwhile performing PRNT. In total, 735 (80.9%) sera were positive for measles IgG and 882 (97.0%) were positive for rubella IgG (Table 2).

The measles antibody prevalence was higher in women, although the results were not statistically significant. Due to the recent vaccine campaign, the measles antibody prevalence showed no significant difference in any of the groups; however, a difference was visible in the group aged 11–15 years. Using the regression analysis model, the seropositivity rate was not correlated to age, which was statistically significant ($p < 0.001$).

Table 1 PRNT of measles ELISA IgG equivocal samples in different age groups

Age group (years)	No.	No. of equivocal	PRNT <128	PRNT ≥ 128
6–10	222	28	24	4
11–15	260	49	24	25
16–20	259	33	14	19
21–26	168	10	8	2
Total	909	120	70	50

PRNT, plaque reduction neutralization test.

Table 2 Measles and rubella seroprevalance in different age groups one year after the immunization campaign in Shiraz, Iran (2004–2005)

No.	Age groups (years)	No.	Measles		Rubella	
			Positive (%)	Negative (%)	Positive (%)	Negative (%)
1	6–10	222	179 (80.6)	43 (19.4)	202 (91.0)	20 (9.0)
2	11–15	260	189 (72.7)	71 (27.3)	259 (99.6)	1 (0.4)
3	16–20	259	220 (84.9)	39 (15.1)	258 (99.6)	1 (0.4)
4	21–26	168	147 (87.5)	21 (12.5)	163 (97.0)	5 (3.0)
	Total	909	735 (80.9)	174 (19.1)	882 (97.0)	27 (3.0)

A higher rate of rubella seropositivity (99.6%) was observed in the 11–15 years and 16–20 years age groups compared to the 6–10 years age group (91%); however the difference between groups was not statistically significant ($p > 0.05$). The seropositivity rate for rubella in 262 women of reproductive age (16–26 years) was 98.9%.

Discussion

The control of vaccine-preventable diseases, including measles elimination, is a high priority in the Eastern Mediterranean Region.[9] These countries must have high-quality immunization activities, including routine and campaign vaccinations, and they must have improved surveillance. These are essential if the regions are to achieve measles elimination by 2010.[9]

In 2003, our country conducted a nationwide campaign targeting 5–25 year-olds with a combined measles and rubella vaccination program, thereby vaccinating some 33.4 million people. Vaccine administration coverage of approximately 100% was reported among individuals aged 5–25 years in Shiraz. The incidence of measles has shown a remarkable decline in our country in recent years due to the routine administration of live attenuated vaccines at the ages of 1 and 6 years, as well as the recent vaccination campaign.[5]

To monitor the impact of this campaign on measles and rubella susceptibility in the target age groups, we collected 909 serum samples in 2004–2005 from individuals aged 6–26 years, and screened them for measles and rubella antibodies.

In this survey, age-related seropositive prevalence against measles reached 80.6% (6–10 years group), 72.7% (11–15 years group), 84.9% (16–20 years group), and 87.5% (20–26 years group). In a previous study reported in Shiraz in 2001, the measles antibody was shown to be positive in 60.8% of cases at 6 years of age, 45% at 10 years of age, and 96.8% at 15 years of age (due to the administration of an additional booster dose of measles vaccine at the latter age).[5] According to these data, a significant increase in seropositive prevalence was observed after the catch-up campaign. However, it was significantly lower than the rate of seroconversion required to achieve $\geq$95% coverage for the elimination of measles.[9] This primary failure after the campaign could be explained by influences such as the nutritional status of children, acute diseases during vaccination, race, environmental factors, sex, and immunity status of those being vaccinated.[5] Additionally, it is estimated that, worldwide, one out of three vaccine injections is not delivered safely.[10]

Maintaining high population immunity can interrupt endemic transmission of the measles virus,[11] but accumulation of susceptible populations represents the greatest risk to measles elimination.[12,13] It has been documented, due to its exceedingly high infectivity, that measles has been observed in individuals with primary, as well as secondary vaccine failures, even when vaccination rates have exceeded 99%.[14] This group of persons would be the most likely to support viral transmission in the absence of disease.[15] Therefore, achieving and maintaining $\geq$95% seropositivity is critical to prevent transmission of measles.[16]

Our data also show that the age-related seropositive prevalence against rubella after the campaign reached 91% (6–10 years group), 99.6% (11–15 years group), 99.6% (16–20 years group), and 97% (21–26 years group). Among the 262 women of reproductive age (16–26 years), the seropositivity rate was 98.9%. However, according to our previous study in Shiraz (2001), in the absence of a rubella vaccination program, seropositivity was 30%, 61% and 94.2% in individuals at 6, 10 and 15 years of age, respectively (unpublished data).

Taken together, these data indicate that the rate of seropositivity to rubella virus in the population studied is high, and suggest that vaccination has been successful in Shiraz, especially in women of childbearing age, thereby preventing congenital rubella infection.

These results show that the success rate of measles vaccination in the national measles–rubella campaign of 2003 in Shiraz among the target population was significantly lower than expected, while for rubella it was excellent. Therefore, it seems that an increase in immunization coverage is needed, and administration of a second dose of measles vaccine would be necessary to interrupt the endemic transmission of the measles virus. Hence, an active and case-based surveillance program, laboratory confirmation of all suspected cases, the maintaining of a routine vaccination program, and follow-up of the campaign in order to detect populations that are susceptible to measles, are necessary in order to effectively control measles in Iran.

Acknowledgments

The authors would like to thank Dr Davood Mehrabani for editorial assistance.

Conflict of interest: No conflict of interest to declare.

References

1. World Health Organization. *The world health report 2005: make every mother and child count*. Geneva: World Health Organization; 2005.
2. World Health Organization. Strategies for reducing global measles mortality. *Wkly Epidemiol Rec* 2000;**75**:409—16.
3. Robertson SE, Featherstone DA, Gacic-Dobo M, Hersh BS. Rubella and congenital rubella syndrome: global update. *Rev Panam Salud Publica* 2003;**14**:306—15.
4. Banatvala JE, Brown DW. Rubella. *Lancet* 2004;**363**:1127—37.
5. Karimi A, Arjomandi A, Alborzi A, Rasouli M, Kadivar MR, Oboodi B, et al. Prevalence of measles antibody in children of different ages in Shiraz, Islamic Republic of Iran. *East Mediterr Health J* 2004;**10**:468—73.
6. Pannuti CS, Morello RJ, de Moraes JC, Curti SP, Afonso AM, Camargo MC, et al. Identification of primary and secondary measles vaccine failures by measurement of immunoglobulin G avidity in measles cases during the 1997 São Paulo epidemic. *Clin Diagn Lab Immunol* 2004;**11**:119—22.
7. Bellini WJ, Sever JL. Measles, mumps, and rubella. In: Spector S, Hodinka RL, Young SA, editors. *Clinical virology manual*. Third ed. Washington DC: ASM Press; 2000. p. 501—12.
8. Chen RT, Markowitz LE, Albrecht P, Stewart JA, Mofenson LM, Preblud SR, et al. Measles antibody: reevaluation of protective titers. *J Infect Dis* 1990;**162**:1036—42.
9. Gaafar T, Moshni E, Lievano F. The challenge of achieving measles elimination in the Eastern Mediterranean Region by 2010. *J infect Dis* 2003;**187**(Suppl 1):S164—71.
10. Duclos P, Hofmann CA. Immunization safety: a priority of the World Health Organization's Department of Vaccines and Biologicals. *Drug Saf* 2001;**24**:1105—12.
11. Fine PE. Herd immunity: history, theory, practice. *Epidemiol Rev* 1993;**15**:265—302.
12. Chen RT, Weierbach R, Bisoffi Z, Cutts F, Rhodes P, Ramaroson S, et al. A 'post-honeymoon period' measles outbreak in Muyinga sector, Burundi. *Int J Epidemiol* 1994;**23**:185—93.
13. Kambarami RA, Nathoo KJ, Nkrumah FK, Pirie DJ. Measles epidemic in Harare, Zimbabwe despite high measles immunization coverage rates. *Bull World Health Organ* 1991;**69**:213—9.
14. Gustafson TL, Lievens AW, Brunell PA, Moellenberg RG, Buttery CM, Sehulster LM. Measles outbreak in a fully immunized secondary-school population. *New Engl J Med* 1987;**316**:771—4.
15. Muller CP. Measles elimination: old and new challenges. *Vaccine* 2001;**19**:2258—61.
16. Cutts FT, Henao-Restrepo A, Olive JM. Measles elimination: progress and challenges. *Vaccine* 1999;**17**(Suppl 3):S47—52.